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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/393,579	09/09/99	KECZER S	IR98-7410

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1627	6

DATE MAILED: 05/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File copy

Office Action Summary

Application No.	Applicant(s)
09/393,579	De Keczer et al.
Examiner	**Art Unit**
Bennett Celsa	1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 20, 2001*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above, claim(s) *2-13, 17, 18, 20, 31, 34-36, 45, and 47-56* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 14-16, 19, 21-30, 32, 33, 37-44, and 46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Status of the Claims

Claims 1-56 are currently pending.

Claims 2-13, 17-18, 20, 31, 34-36, 45 and 47-56 are withdrawn from further consideration.

Claims 1, 14-16, 19, 21-30, 32, 33, 37-44 and 46. are under consideration. .

Election/Restriction

1. Applicant's election without traverse of Group III (claims 14-16, 19-30, 32-44 and 46) in Paper No. 5 is acknowledged.

2. Applicant's further election of species , in Paper No.5 of :

a. α-bromoacetylbenzoic acid (BABA) as the "protected alkylating agent".

b. phosphine as the "disulfide reducing agent";

c. alkaline phosphatase as the "activating agent capable of deprotecting to the protected alkylating agent"; and

d. an antibody as the "reagent capable of specifically binding to modified homocysteine", is acknowledged, which reads on claims 1, 14-16, 19, 21-30, 32, 33, 37-44 and 46. Because applicant did not distinctly and specifically point out the supposed errors in the election of species requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)) . It is noted that the sake of expediency and compact prosecution, claim 1 was included in the elected invention since claim 14 is dependent thereon.

3. Claims 2-13, 17-18, 20, 31, 34-36, 45 and 47-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention..

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 15,16,19, 32, 44 and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claims 32 and 44, use of the term "ligand" and "receptor" for their proposed ability e.g. "capable of specifically binding to said modified homocysteine to form an immunocomplex" is not understood since it appears that "ligand" and "receptors" must correspond to an antibody. This is especially true in light of the specification definition of "immunocomplex" (page 12, lines 30-37) which appears to require the presence of an antibody. Accordingly, the presence of an antibody appears to be an "essential limitation" required in the claims. See MPEP § 2172.01.

B. In claims 1, 19, 32 and 44, "a protected alkylating agent" is indefinite as to what portion of the "alkylating agent" (e.g. amino, sulfhydryl, carboxyl etc) is being protected and from what chemical conditions and/or reaction protection is being sought.

C. In claims 1, 15 and 16, "The reagent" lacks clear antecedent basis.

D. In claims 15, 19, 32, 44 and 46, "chemically modifying homocysteine" or "homocysteine is modified by a reagent" lacks metes and bounds regarding the type of homocysteine modifications within the scope of the claim and the resulting homocysteine structure.

E. In claim 46, the types of modification, the means of modification of homocysteine is indefinite as is the metes and bounds regarding the chemical structure corresponding to "the reagent" and its precursor.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1 and 14 are rejected under 35 U.S.C. 102(b,e) as being anticipated by Metzger et al. US Pat. No. 5,700,910 (12/97)..

Metzger et al. disclose a composition comprising a "disulfide reducing agent" (e.g. Zn in HCL/H2SO4: see col. 2, lin 41) and a "protected alkylating agent" of formula III (e.g. see col. 2, line 45) which anticipates the presently claimed invention. It is noted that intended use limitations are not given patentable weight and compound structure within the present claim scope must inherently possess functionally claimed characteristics (E.g. "deprotection of said reagent is catalyzed by an enzyme").

9. Claims 1, 14-16, 19, 21-30, 32, 33, 37-44 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated or in the alternative as being obvious over Van Atta et al. US Pat. No. 5,478,729 (12/95)..

Van Atta et al. disclose compositions, kits and assays for performing immunodetection of homocysteine in a sample. (E.g. see abstract; patent claims). The assays can be performed homogeneously or heterogeneously using solid supports (e.g. beads such as glass beads; see col.

5). The use of "modifying reagents" especially "alkylating agents" which are preferred and most preferentially the use of α-bromoacetylbenzoic acid (BABA) as the "protected alkylating agent" is specifically disclosed, exemplified and claimed (e.g. see col. 9, lines 20-25; patent claims 10, 25 etc.. It is noted that both BABA (e.g. example IV) and modified BABA (e.g. BABA-N-hydroxysuccinamide ester: see col. 21) constitute "protected alkylating agents" which are within the scope of the presently claimed invention. It is further noted that if a compound is clearly within the scope of the presently claimed invention; claimed functional characteristic must inherently flow therefrom (e.g. "deprotection of said reagent is catalyzed by an enzyme ").

Additionally the patent discloses "releasing agents" particularly "disulfide reducing agents" with disclosed and exemplified phosphines being most preferred (e.g. see col. 15; Example IV and TCEP).

Accordingly, the reference clearly anticipates claims 1 and 14-16 which merely require a "protected alkylating agent alone or further combined with a "disulfide reducing agent" (e.g. TCEP).

With regard to present claims 32 and 33 which recite a homocysteine assay requiring a sample to be contacted with "a protected alkylating reagent" and a "ligand" that is capable of "specifically binding to a "modified homocysteine" to form an immunocomplex and further comprising a disulfide reducing agent; it is initially noted that if "ligand" is interpreted as being an antibody, the reference, as discussed above would anticipate claims 32 and 33. It is further noted

that the reference specifically teaches the incorporation of a "ligand" as part of the "modifying agent" (e.g. see col. 14 bottom) which would alternatively anticipate this claim language.

To the extent that the presently claimed inventions are drawn to kits in which the individual components are separate or combined it is noted that the reference specifically is addressed to kits (E.g. see col. 20; patent claims 27-27). To the extent that the kit claims and/or methods further require the presence of an "activating agent capable of deprotecting to the protected alkylating agent" (e.g. alkaline phosphatase) it is noted that the patent reference teaches the use of "alkaline phosphatase" (e.g. Hcy-ABA-AP) in generating antibodies (e.g. see col. 21; and bottom of col. 22-top of col. 23) and thus would anticipate or render obvious the presence of alkaline phosphatase in kit form (e.g. claims 19, 26). With regard to the presence of "alkaline phosphatase" as part of the immunological assay per se it is noted that the use of "enzymes such as alkaline phosphatase" as a preferred "label" (e.g. see col. 5, lines 30-40) and the use of these enzymes (e.g G-6Ph dehydrogenase) in the liquid assay (e.g. see bottom of col. 18-top of col. 19) would either anticipate or render obvious the incorporation of alkaline phosphatase in solution with the protecting alkylating agent, antibody etc. as found in the presently claimed invention. The use of microtiter well plates are disclosed (E.g. see col. 24, line 44).

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1, 14-16, 19, 21-30, 32, 33, 37-44 and 46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 5,478,729. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claims disclose, compositions, kits and methods of use thereof comprising "modifying agents" particularly alkylating agents (e.g ketones substituted at alpha position by halogens) , releasing agent (e.g. reducing agents), antibodies and labels which can be selected from 5 different types one of which are enzymes (e.g. see patent claim 13) in solution with or without supports. In this regard, BABA as being the ketone substituted at the alpha position by halogen; phosphines as disulfide reducing agents; and alkaline phosphatase for use in kits and assays are either disclosed or specifically exemplified as being preferred embodiments (e.g. see examples; bottom of col 15, col. 19 ; bottom of col. 20 to top of

col. 21; col. 13, lines 25-30; col 5. Accordingly, the patent claim reference would render obvious the presently claimed invention.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat (art unit 1627), can be reached at (703)308-0570.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1627)

May 1, 2001

BENNETT CELSA
PRIMARY EXAMINER